Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Current Research in Translational Medicine 69 (2021) 103284

Available online at ScienceDirect www.sciencedirect.com

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Letter to the editor

A simple score (Biovid-19) based on biological parameters predicts transfer to intensive care units and death in COVID-19 patients

Background

The COVID-19 pandemic, due to SARS-CoV2 infection, was characterized in France by a first wave of patients in the spring of 2020, followed by the current second wave beginning in October 2020. The clinical spectrum of SARS-CoV2 infection is broad, ranging from asymptomatic disease to severe pneumonia with respiratory failure, leading to intensive care unit (ICU) requirement in 14 % of the cases and to an overall estimated death rate around 2 % [1]. Some studies focused on mortality risk factors in patients with COVID-19 and identified age, comorbidities and biological parameters [2]. The relevance of common biological parameters is still to determine, and a scoring system relying on biological features at admittance to predict disease evolution would be highly useful. We present here the result of a monocentric study based on two cohorts, each corresponding to the epidemic waves of spring and fall/winter respectively. The first retrospective cohort of 154 patients, admitted in conventional or intensive care units, identified 3 biological relevant risk factors of increased mortality among the 36 analyzed: plasmatic sodium, potassium levels, and prothrombin time. This score was then prospectively validated in an independent cohort of 81 patients, showing a strong reliability to identify patients at risk of severe COVID-19 evolution. This biological score, relying on broadly available parameters, is an easy and usable tool to early discriminate high-risk patients that are most likely to benefit from intensive care treatment.

Material and methods

Study design and clinical features

The first retrospective derivation cohort included all consecutive adult patients (≥ 18 years old) admitted from February 21 st, 2020 to March 30th, 2020 in University Hospital (CHU) of Amiens and diagnosed with COVID-19 according to the viral detection of SARS-CoV2 (PCR). The second prospective validation cohort included all consecutive adult patients admitted from October 19th, 2020 to November 17th, 2020 in the same hospital and diagnosed with COVID-19 with a similar test. Clinical and biological data were extracted from electronic medical records. The analyzed biological parameters were collected at hospital admittance (day 0).

This study was approved by the institutional review board of Amiens University Hospital (number PI2020_843_0031, 30th March), and are in accordance with French legislation of non-interventional studies.

Statistical analysis

Student's t-test, receiver operating characteristic (ROC) curve analysis and Kaplan-Meier analysis were used as indicated. Univariate and multivariate analyses were performed using a step-by-step backward Cox regression. $P < 0.05$ was considered as statistically significant.

Results

Patient demographics and baseline characteristics

In the derivation cohort, 154 patients were admitted with confirmed SARS-CoV2 infection in the Amiens hospital. These patients were hospitalized in conventional units (n = 111, 72 %) or ICU (n = 43, 28 %), and 18 of them were transferred from conventional to ICU. The median age at admission was 77 years (range 23–100), 56 % of the patients were male and 44 % female. The median length of stay was 12 days both in conventional care units and ICU. At the time of analysis, 122 patients were alive (79 %) and 32 died (21 %) from SARS-CoV2 infection. The second validation cohort prospectively included 81 SARS-CoV2 patients meeting the same criteria, whose characteristics were not statistically different from the first cohort (data not shown).

Biological markers to identify high risk patients

We then performed survival analyses to determine if biological parameters at diagnosis could predict clinical outcomes. OS was defined as time to death or latest news. To consider the risk of severe clinical worsening, EFS was defined as time to ICU transfer,

Table 1
Biovid-19 score.

Parameter	Range	Score point
Sodium (mmol/L)		
	≤130	2
	]130-135]	1
	>135	0
Potassium (mmol/L)		
	≥5,5	2
	]5,5-5]	1
	<5	0
PT (s)		
	>20	2
	]20-16,8]	1
	≤16,8	0

Interpretation of the proposal score: Patient at high risk of mortality if score ≥2.

http://dx.doi.org/10.1016/j.retram.2021.103284

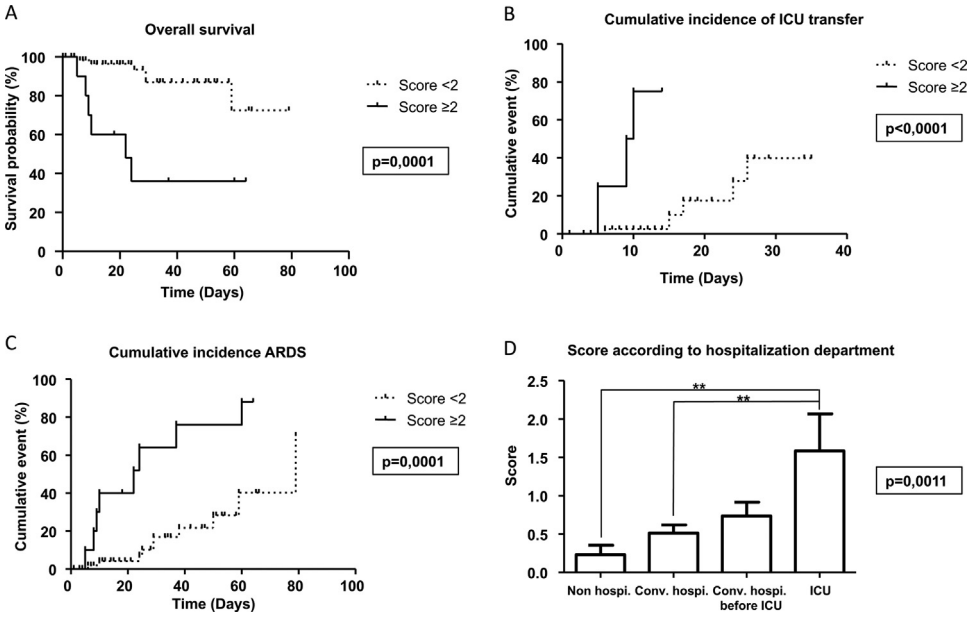

Fig. 1. Overall survival according to the proposal score by the Kaplan Meier method.

death in conventional care units, or latest news. At median follow up, EFS and OS were close to 85 %. Univariate analysis for EFS identified lymphopenia (p = 0.048), hyponatremia (p = 0.003), high uremia levels (p = 0.02) and hypocalcemia (p = 0.01) as risk factors for severe clinical worsening, whereas age had no significant impact (p = 0.53). In multivariate analysis, hyponatremia (HR = 11.7 (95 %CI:3.1–44.2), p < 0.001) and low bicarbonate levels (HR = 5.4 (95 %CI:1.4–21), p = 0.02) negatively affected EFS.

Regarding OS, hyponatremia (p = 0.038), hyperkaliemia (p = 0.005), high creatinine levels (p = 0.049), hyperphosphoremia (p = 0.006), and low O2 saturation (p = 0.01) significantly predicted shorter survival in univariate analysis. There was a trend for prolonged prothrombin time > 16,8 s (p = 0.1). Age was also an adverse prognostic factor for OS (p = 0.008, HR = 1.04 (1.01–1.07)). Then, in multivariate analysis, age (HR = 1.13 (95 %CI:1.04-1.22), p = 0.002), prothrombin time > 16,8 s (HR = 4.62 (95 %CI:1.19-17.94), p = 0.03), hyponatremia (HR = 6.99 (95 %CI:1.83-26.72), p = 0.005), and hyperkaliemia (HR = 12.1 (1.66–87.75), p = 0.01) were independent factors predicting shorter OS.

Easy usable score to predict early survival in COVID-19 patients: Biovid-19

Based on the results of the multivariate analysis presented above, we proposed a simple biological prognostic score including sodium, potassium levels and prothrombin time. 0, 1 or 2 points are assigned to each of the 3 parameters, according to the weight of their respective HR, resulting in a score ranging from 0 to 6 (Table 1). Using ROC analysis, we proposed that a threshold ≥2 predicted poor prognosis with a sensitivity of 80,7 % and a specificity of 93,3 %. Therefore, we independently validated in our second prospective cohort an improved OS with a score <2 (Fig. 1A), showing a strong reliability of Biovid-19 score to predict the risk of death in time-different waves. Interestingly, we also validated that Biovid-19 score predicts clinical worsening, as it prospectively highlighted a significantly lower cumulative incidence of both secondary transfer to ICU and development of Acute Respiratory Distress Syndrome (ARDS) in patients with a score <2 (Fig. 1B and C). Moreover, our score was significantly lower in non-hospitalized patients and patients hospitalized in conventional units compared to patients hospitalized in ICU (Fig. 1D), reflecting the association with severe disease presentation.

Taken together, these data suggest that few common and broadly available biological parameters at admittance can easily and reliably identify patients at risk of severe Covid-19 evolution. We assume that the Biovid-19 prognostic score is useful to early identify high-risk patients requiring close monitoring, and could help guidance for early ICU admittance.

Declarations

Ethics approval and consent to participate : This study was approved by the institutional review board of Amiens University Hospital (number PI2020_843_0031, 30th March).

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Funding

Not applicable.

Authors'contribution

TB and CS designed the research study. TB, CS, GC, ML, OE and AC collected and analysed the data. CF, EB and SC set up the virological diagnosis. RN, JLS, CA, JM managed patients and provided clinical data. TB, CS, GC, ML, AC and LG wrote the paper, which was approved by all the authors.

Declaration of Competing Interest

The authors declare that they have no competing interests.

Acknowledgments

We deeply thank Victor Eonnet for the data management and Corinne Lorriaux for her advices.

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Received 8 February 2021

Available online 4 March 2021